Update on advanced life support and resuscitation techniques

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Purpose of review

This article is a review of the most recent findings in resuscitation techniques in advanced cardiac life support. The article focuses particularly on the period after July 1, 2003, but relevant new findings before this period are also included.

Recent findings

Randomized clinical trial results suggest that the current cardiopulmonary resuscitation and advanced cardiac life support guidelines may need to be modified. Early defibrillation during the electrical phase of cardiac arrest remains the most crucial intervention, but performing cardiopulmonary resuscitation before defibrillation may be more effective, as compared with immediate defibrillation, during the circulatory phase of cardiac arrest. Biphasic waveforms are superior to monophasic damped sine waveforms in achieving defibrillation. Novel cardiopulmonary resuscitation methods that increase negative intrathoracic pressure promote an increase in blood flow return to the heart. These devices have been correlated with improved short-term survival rates during the circulatory phase of cardiac arrest. Vasopressin administration, given alone or in combination with epinephrine, should be considered during the circulatory phase of out-of-hospital cardiac arrest, particularly in patients presenting with asystole as the initial rhythm. Induction of hypothermia during the metabolic phase in cardiac arrest survivors improves 6-month survival rates and neurologic outcomes.

Summary

Strategies to improve the low survival outcomes of cardiac arrest victims are available. Clinical trials testing these strategies suggest benefit from certain interventions but are not definitive. These different therapeutic interventions should be performed in a phase-specific-oriented fashion according to the three-phase time-sensitive model of cardiac arrest.

Keywords

cardiac arrest, out-of-hospital cardiac arrest, ventricular fibrillation, defibrillation, emergency medical systems, cardiopulmonary resuscitation

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Abbreviations

ACLS	advanced cardiac life support
ACD	active compression–decompression device
CA	cardiac arrest
CPR	cardiopulmonary resuscitation
ITD	impedance threshold device
MDS	monophasic damped sine
OHCA	out-of-hospital cardiac arrest
VF	ventricular fibrillation

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Introduction

Out-of-hospital cardiac arrest (OHCA) has become a major epidemiologic and public health challenge in the Western World. The estimated number of cases varies from 184,000 [1] up to 450,000 [2] each year in the United States. In the OPALS study, a detailed prospective evaluation of cardiac arrest in Ontario, Canada, OHCA rates were observed at 0.6 per 1,000 population per year [3]. Independent of the exact number, it is clear that OHCA is responsible for a significant proportion of the death toll in North America and Europe.

The survival rate of OHCA patients to hospital discharge is discouraging. Overall survival is less than 5% in the United States and Canada [1,4]. An optimized defibrillation system in Ontario increased survival rates from less than 4% to 5% [3]. Hamill *et al.* recently reported a survival to hospital discharge rate for OHCA caused by ventricular fibrillation (VF), in the setting of rapid defibrillation, of as high as 40% [5].

The incidence of VF as the initial documented rhythm among patients with OHCA has been reported to be decreasing, while the frequency of pulseless electrical activity (PEA) and asystole seems to be increasing [6]. However, VF is still the predominant rhythm in the first 3 to 5 minutes after OHCA in a public setting [7••].

Three-phase time-sensitive model and appropriate therapeutic interventions

Weisfeldt and Becker [8••] described a three-phase model of cardiopulmonary resuscitation (CPR) to reflect the time-sensitive progression of pathophysiologic re-

sponse to cardiac arrest and its treatment. They propose a phase-specific-oriented treatment to achieve better survival outcomes. The first phase includes approximately the first 4 minutes after the patient collapses and it is called the electrical phase. During this first phase, immediate defibrillation is the appropriate therapy.

The second phase involves approximately minute 4 up to minute 10 after the onset of VF, and it is called the circulatory phase. Restoration of organized electrical activity during this phase does not necessarily result in an adequate contractile response [9,10]. During this phase, promoting cardiac and cerebral oxygen delivery (chest compression/ventilation) and delaying defibrillation seem to yield better survival outcomes. Initiating CPR before restoration of organized electrical activity may promote the washout of deleterious metabolic factors and may allow oxygen delivery to already ischemic tissues.

The third phase begins approximately 10 minutes after the onset of VF and it is called the metabolic phase. During this phase, the consequences of prolonged periods of tissue ischemia may resemble a state of sepsis, resulting in release into circulation of tumor necrosis factor, endotoxins, and cytokines, all of which suppress myocardial contractility [11].

Early defibrillation–the first 4 minutes

During the electrical phase of the cardiac arrest (CA) model, the crucial therapy is early defibrillation. The efficacy of electrical countershock for VF decreases dramatically with time. Defibrillation success for VF is practically 100% in the electrophysiology laboratory after induction of this rhythm. The success decreases to about 80 or 90% after 60 seconds of sustained VF and after 20 minutes of sustained VF, restoration of a perfusing rhythm is rare [12].

Valenzuela *et al.* [7••] reported that 105 of 148 persons experiencing OHCA in US casinos had ventricular fibrillation as the initial documented rhythm. Of these 105 persons, 90 had witnessed CAs caught on film by video surveillance systems, and 53% of these patients survived to discharge from the hospital. The interval from collapse to first defibrillation, utilizing automated external defibrillators (AED), was 4.4 ± 2.9 minutes. The reported survival rate was 74% for those who received their first defibrillation during the first 3 minutes after collapse and 49% for those who received their first defibrillation after more than 3 minutes.

These studies support the concept that early defibrillation is useful and effective, if applied within 5 minutes of onset of OHCA.

Biphasic and monophasic shocks for transthoracic defibrillation

Biphasic defibrillation waveforms are characterized by an initial positive current flow followed by a reversal to negative current flow. Animal studies showed that biphasic waveforms had 30 to 56% lower defibrillation thresholds than monophasic waveforms for VF or ventricular tachycardia of short duration. For VF or ventricular tachycardia of 10 minutes, the biphasic waveforms had 38 to 56% lower defibrillation thresholds [13,14].

Implanted defibrillators and semiautomatic external defibrillators deliver biphasic waveform shocks. A meta-analysis of six randomized controlled trials [15–20] comparing biphasic and monophasic shocks for transthoracic defibrillation during electrophysiology procedures or implantable cardioverter/defibrillator testing was performed by Faddy *et al.* [21]. When compared with 200 joules (J) monophasic damped sine (MDS) defibrillation, 200 J biphasic defibrillation reduced the risk of first shock failure by 81% (RR 0.19; 95% CI 0.06 to 0.60), defined by Faddy *et al.* as persistent VF or hemodynamically unstable ventricular tachycardia as well as first post-shock asystole.

The ORBIT trial compared a special type of biphasic waveform called rectilinear biphasic defibrillation to MDS defibrillation waveforms in OHCA patients receiving advanced cardiac life support (ACLS) in Toronto, Ontario. It showed that the rectilinear biphasic waveform at 120J and 200J was superior to 200J and 360J MDS waveform shocks using step-up energy levels for conversion of VF or pulseless ventricular tachycardia to an organized rhythm during ACLS for OHCA [22]. Although a higher success rate in restoring electrical activity was noted, the survival rates to hospital admission and to hospital discharge were comparable to the MDS waveform group. This may have been related to the fact that these patients were in the circulatory phase of CA and immediate defibrillation was performed rather than CPR before defibrillation.

Biphasic waveform defibrillation for every person with OHCA or in-hospital CA seems reasonable. Although there are no clinical data comparing biphasic against MDS defibrillation in the electrical phase of CA, we believe that biphasic defibrillators should become the standard of care in external defibrillation.

Cardiopulmonary resuscitation before defibrillation during the circulatory phase

Animal studies showed that prolonged periods of untreated VF (> 7 minutes) can be more effectively treated if 5 minutes of CPR plus epinephrine administration precede defibrillation, compared with defibrillation first [23,24]. Wik *et al.* [25] conducted a randomized clinical trial in which patients with OHCA received either standard care with immediate defibrillation or 3 minutes of basic CPR by ambulance personnel before defibrillation. For the 119 patients where the emergency medical system response time, calculated from time of dispatch of the first ambulance to arrival on the scene (as registered

on-line by a central computer system in the dispatch center), was more than 5 minutes, more patients in the CPR-first group than in the defibrillation-first group achieved return of spontaneous circulation, 58% versus 38% ($P = 0.04$). Survival to hospital discharge was 22% versus 4%, respectively ($P = 0.006$) and 1-year survival was 20% versus 4% ($P = 0.01$). No significant difference was noted in the group where the EMS response was less than 5 minutes.

In the circulatory phase, CPR for 3 minutes before defibrillation is reasonable. Additional studies to verify this benefit are needed. The interval after which CPR first becomes indicated and the optimum duration of CPR first are not known.

Active compression–decompression cardiopulmonary resuscitation and the inspiratory impedance threshold device

Effective CPR should be performed during the circulatory phase of CA. To improve survival, two devices have been developed: the active compression–decompression device (ACD) and the inspiratory impedance threshold device (ITD). When the chest wall recoils, in the decompression phase of CPR, a negative intrathoracic pressure is created that promotes venous return and filling of the cardiac chambers. The ACD is a hand-held cup-like device created to actively decompress the chest during CPR [26]. Clinical trials show conflicting results as to the benefit of the ACD. Plaisance *et al.* [27] demonstrated a significant benefit from the ACD as compared with standard CPR when applied by trained personnel. However, other trials were not able to demonstrate improved clinical outcomes with the ACD device [28].

The ITD is a small, 35-mL device that fits at the end of an endotracheal tube or face mask. It has a valve that allows the rescuer to actively ventilate the patient, but it impedes inspiratory airflow during chest decompression with a valve that opens only when the airway pressure is more negative than about –15 cm H_2O during the CPR decompression phase. This creates a small vacuum within the chest, increasing the venous return to the heart [29]. The ACD and ITD can work together to increase and maintain negative intrathoracic pressure during chest decompression.

Plaisance *et al.* [30•] randomized patients to receive ACD CPR with either an ITD or a sham valve. Short-term survival (24 hours) was 32% in the active valve group versus 22% in the sham valve group ($P = 0.02$); 6/10 survivors in the active valve group compared with 1/8 survivors in the sham group had normal neurologic function at hospital discharge ($P = 0.1$).

A second trial of ACD and ITD versus control in OHCA showed improved short-term outcomes in patients with VF as well as asystole. Patients with witnessed CA due to VF had 1- and 24-hour survival rates of 68% and 58%, respectively, with ACD+ITD CPR versus 27% and 23%, respectively, in patients receiving standard closed-chest compression CPR ($P = 0.002$ and 0.009, respectively) [31•]. The ACD is approved for use, and it is currently a class II b indication in the AHA ACLS guidelines [32].

Circumferential compression of the chest with use of a pneumatic vest increases systolic and diastolic arterial blood pressure as well as coronary blood flow [33]. The effect of vest CPR on survival from CA is currently under study. Another method to improve blood return to the heart during the decompression phase is interposed abdominal counterpulsation. A randomized clinical trial of interposed abdominal counterpulsation for cardiac arrest did not show survival benefit [34].

During the circulatory phase of CA, effective CPR should be performed by optimizing the negative intrathoracic pressure during the decompression phase. The use of ACD plus ITD with appropriate prior training should be considered.

Hyperventilation induced hypotension during cardiopulmonary resuscitation

Hyperventilation provided during CPR increases the proportion of time when intrathoracic pressure is positive, limiting the opportunity to promote venous return of blood to the heart during decompression [35,36]. In an observational study of CPR by professional trained personnel after intubation, the patients were ventilated at a rate of 30 ± 3.2 times per minute. None of the patients survived in this clinical study. The percentage of time in which positive intrathoracic pressure was recorded was between 45 and 50% [37•].

In a companion animal study [37•], 9 pigs were ventilated at 12, 20, and 30 times per minute during VF. A lower mean intrathoracic pressure (7.1 ± 0.7 mmHg versus 17.5 ± 1.0 mmHg) and a higher coronary perfusion pressure (23.4 ± 1.0 mmHg versus 16.9 mmHg) was measured when the pigs were ventilated at 12 times/min as compared with 30 times/min.

These observations highlight the risks of overventilation, which include interruption of chest compressions, inadequate release of the airway bag during expiration (leading to residual positive and expiratory pressure (PEEP)), and inadequate time for decompression-related negative thoracic pressure. Patients should not be ventilated at a rate greater than that recommended in the ACLS guidelines, 10 to 12 times/min before intubation and 12 to 15 times/min after intubation [32].

Comparison of vasopressin and epinephrine for out-of-hospital cardiac arrest

The observation that CA survivors had higher levels of endogenous vasopressin compared with the patients that died led to further investigation in resuscitation treatment [38]. In a clinical trial, 1219 patients with OHCA were randomized to receive up to two injections of either vasopressin (40 IU) or epinephrine (1 mg) followed by additional treatment with epinephrine, if appropriate. The endpoints were survival to hospital admission and to hospital discharge. There were no significant differences in outcomes in the patients found in VF or PEA at the time of the CA. However, rates of hospital admissions and discharges in the patients with asystole as the presenting rhythm treated with vasopressin were significantly higher than with epinephrine, 29% versus 20.3%, respectively, for hospital admissions and 4.7% versus 1.5%, respectively, for hospital discharges. This hospital discharge rate reported for asystolic OHCA is the highest reported in the literature.

In the group of patients receiving vasopressin before further administration of epinephrine, the survival rate was higher than in the group receiving more than two doses of epinephrine without vasopressin ($P = 0.007$) [39••]. This effect may be due to the fact that vasopressin may be more effective than catecholamines in the setting of acidosis [40].

Vasopressors are indicated during the circulatory phase of the CA model, and they should be administered very carefully during the metabolic phase. Vasopressin may be considered during the circulatory phase of CA when large amounts of vasopressors are anticipated to be needed, especially if asystole is the initial recorded rhythm. Large amounts of epinephrine are likely deleterious, especially in the metabolic phase of CA [41].

Amiodarone for shock-resistant ventricular fibrillation and recurrence of ventricular fibrillation

Persistent and especially recurrent VF are relatively common in OHCA due to VF [42].

Ventricular fibrillation that persists after three or more external defibrillation shocks or VF that recurs more than 5 seconds after a successful defibrillation shock is labeled shock-resistant VF. The ARREST trial in 1999 showed that patients treated with amiodarone with shock-resistant VF were more likely to survive to hospital admission compared with the placebo group (44% versus 34%, respectively, $P = 0.03$) [43]. In the Amiodarone vs Lidocaine in Ventricular Fibrillation Evaluation (ALIVE) trial, a significant increase in the proportion of patients surviving hospital admissions was demonstrated in the amiodarone group when compared with the lidocaine group (22.8% versus 12%, $P = 0.009$). The time from dispatch of the EMS to administration of amiodarone (median time 24 minutes) had an impact on survival to hospital admission, with early administration of the drug yielding better results. When the presenting rhythm was VF, 6.4% of the patients in the amiodarone group compared with 3.8% in the lidocaine group survived to hospital discharge ($P = 0.32$) [44].

Van Alem *et al.* [45] reported at least one VF recurrence in 79% of the 380 patients with VF OHCA. The incidence of refibrillation was independent of the underlying cardiac disorder, the time of defibrillation, the defibrillation waveform, and many other variables. An inverse relation between recurrence of VF and survival was noted. These authors suggest that aggressive use of antiarrhythmic drugs may prevent the incidence of refibrillation.

We recommend considering the early use of amiodarone for patients with OHCA due to shock-resistant VF and for patients with recurrence of ventricular fibrillation during the circulatory phase of CA. Amiodarone may be effective if given after successful defibrillation to prevent refibrillation, in either the circulatory or the metabolic phases of CA, but clinical trials for this indication have not been performed.

Induction of hypothermia after cardiac arrest

Hypothermia induction during the metabolic phase of CA has been shown to improve medium-term survival and neurologic outcomes.

In an *in vitro* model, ischemic cardiomyocyte death was reduced by 60% after lowering the temperature to 25°C before reperfusion. Reperfusion, with its oxidant burst, rather than ischemia alone is responsible for cardiac cell death, at least in this cellular model [46]. Hypothermia is also associated with a controlled decrease in intracranial pressure. Two prospective randomized studies reported improved outcomes when deliberate hypothermia, 32 to 34°C, was induced in patients resuscitated from cardiac arrest [47,48]. In a European trial, 75 of the 136 patients (55%) in the hypothermia group had a favorable neurologic outcome 6 months after CA as compared with 54 of the 137 patients (39%) in the normothermia group (RR 1.40; 95% CI, 1.08 to 1.81). Mortality at 6 months was 41% in the hypothermia group as compared with 55% in the normothermia group (RR, 0.74; 95% CI, 0.58 to 0.95) [47]. A similar trial conducted in Australia reported a better survival to hospital discharge rate with a sufficiently good neurologic function in the hypothermia group (49%) compared with the normothermia group (26%, $P = 0.046$) [48]. In this study, discharge home or to a rehabilitation facility was regarded as a good outcome, whereas death in the hospital or discharge to a long-term

nursing facility, regardless of the patient's state of consciousness, was regarded as a poor outcome. Hypothermia was not associated with adverse effects in either trial.

The routine use of hypothermia should be considered during the metabolic phase of CA. The optimum time to start inducing hypothermia, the duration of treatment, the optimal technique, and the ideal method of rewarming are all questions that still remain unanswered.

Conclusion

Overall hospital discharge survival rates for OHCA are less than 5%. Understanding the Weisfeldt and Becker three-phase model should allow emergency medical systems to better direct therapeutic maneuvers during resuscitation. In the electrical phase, early defibrillation with biphasic waveforms should be the standard of care. During the circulatory phase, effective CPR that allows adequate venous return to the heart is paramount. ACD CPR with the use of an ITD and avoidance of hyperventilation-induced hypotension may help to achieve this goal. Pharmacological treatment during the circulatory phase includes the early use of amiodarone for shock-resistant VF and/or refibrillation. Vasopressin should be considered when high doses of vasopressors are suspected to be needed, especially if asystole is documented. High doses of epinephrine should be avoided because the deleterious effects of this intervention probably outweigh its benefits. In the metabolic phase, hypothermia may be helpful for survivors of OHCA.

Clinical trials testing optimum applications of these principles, especially used in combination, are needed to better define the ideal methods of ACLS.

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